

**Claim rejections under 35 U.S.C. § 112, second paragraph**

The Examiner rejected claims 1-20 as being indefinite. Claims 1-20 have been canceled and thus this ground of rejection is moot. Accordingly, Applicants respectfully request withdrawal of this ground of rejection.

**Claim rejections under 35 U.S.C. § 102(e) or under 35 U.S.C. § 103(a) over Brown et al.**

Claims 1, 2, 4-7, and 17-20 have been rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Brown et al. (U.S. Patent No. 5,907,522). The cancellation of these claims renders this ground of rejection moot. However, in so far as the Examiner considers this ground of rejection to be applicable to any claims presently in the application upon entry of this amendment, it is respectfully traversed.

The Examiner alleges that Brown et al. disclose a method for retaining a minute droplet on a substrate. According to the Examiner, Brown's method includes retaining the minute droplet in a layer coated over a surface of the substrate. The minute droplet is in contact with the substrate and the minute droplet and the liquid separate into two phases. (Col 7, lines 47-54). The Examiner also alleges that Brown et al. teach that the layer coated over the surface of the substrate is hydrophobic polymers lubricants, and films (Col, 7, lines 50-54) and the layer is applied by spraying or coating uncured polymers onto the substrate (Col 12, lines 11-12). The Examiner asserts that it would have been known to one of ordinary skill in the art that it is an inherent property of hydrophobic polymers, lubricants, and films that they would be applied as liquids.

Applicants submit that in Brown et al. the droplet is only deposited on the surface of a

support and the droplet is not, as in the present invention, surrounded by a liquid layer. In contrast, the present invention enables reactions requiring a lengthy time period because the evaporation of the minute droplet is reduced. To the contrary, in Brown et al., the droplet is only deposited on the surface of a support. The droplet is not surrounded on all surfaces not in contact with the support by a liquid layer. In Brown et al., it contrast to the present invention, the droplet can be readily evaporated. In fact, Brown et al. teach the desired evaporation on Col. 9, lines 41-45: “[a]fter formation of the array, the support is treated to evaporate the liquid of the droplet forming each region, to leave a desired array of dried, relatively flat regions. This drying may be done by heating or under vacuum.” (Emphasis added.) Thus, Applicants submit that Brown et al. teach away from the present invention as Brown et al. aim for evaporation of the droplet, whereas the present invention aims to protect against evaporation.

With respect to the Examiner's statement that Brown et al. teach the layer coated over the surface of the substrate with hydrophobic polymers, which would be applied as liquids. Applicants submit, as discussed above, that Brown et al. do not teach a liquid layer to prevent evaporation. Brown et al. merely teach that this modified surface (coated with hydrophobic polymers) acts to prevent spreading of the droplet applied to the surface by hydrophobic interaction with the droplet, so that the droplet can be deposited exactly at the defined position on the support surface to form a high-density array. See Brown et al. Col. 7, lines 46-48 “[i]n another embodiment, the surface has or is formed to have a relatively hydrophobic character, i.e. one that causes aqueous medium deposited on the surface to bead.” See also Brown et al. Col. 8, lines 14-17 “[a]t a given bead size, i.e. volume, the tendency of the liquid to flow onto the surface will be balanced by the hydrophobic surface interaction of the bead with the support

surface, which acts to limit the total bead area on the surface. . . .” Thus, applicants submit that the layer of hydrophobic polymers as taught be Brown et al., whether applied as a liquid or not, does not teach providing a liquid layer surrounding all surfaces of the minute droplet that are not in contact with either the substrate or covering.

With respect to the Examiner's statement that Brown et al. teach an oily hydrophobic lubricant, Applicants submit that as discussed above, this modified surface (coated with hydrophobic polymers) acts to prevent spreading of the droplet applied to the surface by hydrophobic interaction with the droplet, so that the droplet can be deposited exactly at the defined position on the support surface to form a high-density array. Accordingly, Brown et al. do not point to the formation of an oily liquid layer on the support surfaces. As discussed above, Brown et al. teach treating the support to evaporate the liquid of the droplet. This drying process would be impossible to perform if the surface is covered with the oily liquid, as in the case of the present invention, because the droplet may be buried into the oily liquid and inhibited from evaporating.

The Examiner alleges that Brown et al. disclose the surface of the substrate having water repellency. Although Applicants agree that Brown et al. teach a water repellency surface, Applicants submit that Brown et al. fail to teach a process for reducing evaporation of a minute droplet. Indeed, as previously discussed Brown et al. teach evaporation.

With regard to the Examiner's comments regarding Brown et al.'s disclosure of a covering, Applicants submit that Brown et al. do not teach providing a covering over a liquid layer that either surrounds all surfaces of a minute droplet that are not in contact with the substrate or that surround all surfaces of a minute droplet that are not in contact with the substrate

or the covering. Brown et al. merely teach providing a covering over small samples previously placed onto an array surface. Col 16, lines 61-62. Thus, Applicants submit that, as discussed above, Brown et al. do not teach or suggest the use of a liquid layer, and, therefore, do not teach or suggest providing a cover over a liquid layer either surrounding all surfaces of a minute droplet that are not in contact with the substrate or surrounding all surfaces of a minute droplet that are not in contact with the substrate or the covering. .

The Examiner also alleges that Brown et al. disclose another aqueous solution retained in the vicinity of a minute droplet. Applicants submit that Brown et al., as discussed above, do not teach providing a liquid layer, let alone, teach providing an aqueous solution into the liquid layer.

Applicants respectfully submit that Brown et al. do anticipate the claims of the present invention nor render them obvious. Accordingly, Applicants request withdrawal of this ground of rejection.

**Claim rejections under 35 U.S.C. § 102(e) over Brown et al.**

Claims 8, 9, and 12 have been rejected under 35 U.S.C. 102(e) as anticipated by Brown et al. (U.S. Patent No. 5,907,522). The cancellation of these claims renders this ground of rejection moot. However, in so far as the Examiner considers this ground of rejection to be applicable to any claims presently in the application upon entry of this amendment, it is respectfully traversed.

The Examiner alleges that Brown et al. teach a reaction method comprising the steps of retaining a minute droplet on a coated substrate wherein said minute droplet and coating separate

into two phases (Col. 7, lines 46-54); covering the surfaces of said liquid layer with a covering (Example 1, col. 16, line 62), and effecting a reaction in said minute droplet (Example 1, lines 57-65). Applicants respectfully submit that although Brown et al. teach in Example 1 a reaction, Brown et al. do not teach nor suggest a reaction in a minute droplet protected from reduced evaporation comprising the steps of providing a liquid layer wherein said liquid layer surrounds all surfaces of said minute droplet that are not in contact with said substrate. To the contrary, Brown et al. teach in Example 1 first the addition of DNA to the substrate and then drying of the substrate, "[a]fter the spotting operation was complete, the slides were re-hydrated in a humid chamber for 2 hours, baked in a dry 80°C vacuum oven for 2 hours, rinsed . . . ." Col. 16, lines 31-34). The reaction in Example 1 of Brown et al. then occurs with a cover slip placed over the substrate and occurs in a humidity chamber. Thus, Brown et al. do not teach the use of a liquid layer surrounding the minute droplet to reduce evaporation. Rather, Brown et al. teach first the drying of the substrate having a spotted sample, subsequent addition of a reagent to the top of the dried substrate, and then performing the reaction with a cover in a humidity chamber. There is no teaching or suggestion of providing a liquid layer surrounding all surfaces of said minute droplet that are not in contact with the substrate.

With regard to the Examiner's comments that Brown et al. teach a layer coated on the substrate having a thickness of less than 100  $\mu\text{m}$  (Col. 12, line 10), Applicants submit that Brown et al. do not teach a liquid layer having a thickness of about 100  $\mu\text{m}$  or less. Instead, Brown et al. teach a substrate having a water impermeable backing plus a water permeable film, such film being between about 10 and 1000  $\mu\text{m}$  thick. (Col. 12, lines 3-9). Thus, Brown et al. do not teach, as discussed above a liquid layer, let alone a liquid layer having a thickness of 100  $\mu\text{m}$  or

less.

Applicants respectfully submit that Brown et al. do anticipate the claims of the present invention nor render them obvious. Accordingly, Applicants request withdrawal of this ground of rejection.

**Claim rejections under 35 U.S.C. § 103(a) over Brown et al. in view of Blanchard et al.**

Claims 3 and 12 have been rejected under 35 U.S.C. §103(a) as being obvious over Brown et al. (U.S. Patent No. 5,907,522) in view of Blanchard et al. (U.S. Patent No. 6,028,189). The cancellation of these claims renders this ground of rejection moot. However, in so far as the Examiner considers this ground of rejection to be applicable to any claims presently in the application upon entry of this amendment, it is respectfully traversed.

As previously discussed, Brown et al. do not teach nor suggest providing a liquid layer surrounding all surfaces of a minute droplet that are not in contact with a substrate and/or covering. Applicants further submit that Blanchard et al. also fail in this regard. Blanchard et al. merely teach the use of an ink jet to deposit DNA synthesis reagents onto a glass slide. Applicants, therefore, submit that the combination of Brown et al. and Blanchard et al.'s teachings fail to teach or suggest the present invention.

Applicants respectfully submit that Brown et al. in view of Blanchard et al. do not render the claims obvious. Accordingly, applicants request withdrawal of this ground of rejection.

**Claim rejections under 35 U.S.C. § 103(a) over Brown et al. in view of Sambrook et al.**

Claims 10 and 11 have been rejected under 35 U.S.C. §103(a) as being obvious over

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Brown et al. (U.S. Patent No. 5,907,522) in view of Sambrook et al. (Molecular Cloning: A Laboratory Manual, 2nd Ed., 1992). The cancellation of these claims renders this ground of rejection moot. However, in so far as the Examiner considers this ground of rejection to be applicable to any claims presently in the application upon entry of this amendment, it is respectfully traversed.

As previously discussed, Brown et al. do not teach nor suggest providing a liquid layer surrounding all surfaces of a minute droplet that are not in contact with a substrate and/or covering. Applicants further submit that Sambrook et al. also fail in this regard. Sambrook et al. merely teach the use of various reagents, such as SDS and Denhardt's reagent, to block non-specific reactions. Applicants, therefore, submit that the combination of Brown et al. and Sambrook et al.'s disclosures fail to teach or suggest the present invention.

Applicants respectfully submit that Brown et al. in view of Sambrook et al. do not render the claims obvious. Accordingly, applicants request withdrawal of this ground of rejection.

**Claim rejections under 35 U.S.C. § 103(a) over Stimpson et al. in view of Sambrook et al.**

Claims 13-15 have been rejected under 35 U.S.C. §103(a) as being obvious over Stimpson al. (U.S. Patent No. 5,907,522) in view of Sambrook et al. (Molecular Cloning: A Laboratory Manual, 2nd Ed., 1992). The cancellation of these claims renders this ground of rejection moot. Accordingly, Applicants respectfully request withdrawal of this ground of rejection.

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### CONCLUSION

In view of the foregoing amendments and remarks, it is firmly believed that the subject invention is in condition for allowance, which action is earnestly solicited.

The Office is hereby authorized to charge Deposit Account No. 11-0600 with any additional fees required by this paper or credit any overpayment.

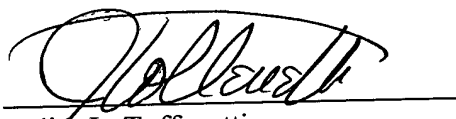
If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned directly at (202) 220-4200.

Prompt and favorable consideration of this Amendment is respectfully requested.

Respectfully submitted,

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Date: June 12, 2000

  
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